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Tumorspheres from *in vitro* transformed cell lines show molecular signatures related to stemness and transformation

E vidence indicates that a subset of cells endowed with high tumorigenic potential and stemness features (cancer stem cells: **E** CSCs) is responsible for tumor initiation and maintenance in several cancers. In this study, we used a tumor cellular model developed in our laboratory from telomerase immortalized human fibroblasts (named cen3tel) and the tumorsphere assay to possibly isolate and characterize CSCs from *in vitro* transformed cells. We found that cen3tel cells were able to form spheres (frequency ~ 2-10%) and sphere cells showed self renewal capacity and Sox2 overexpression, suggesting that in these populations there is a subset of cells with CSC-like features. The characterization of sphere cells revealed that they displayed the activation of pro-survival mechanisms, through the expression modulation of genes as *c-MYC*, *GNL3* and *Notch*, and the tumor suppressor miR-34a, which could favor the growth of cells in suspension upon detachment from a solid support. Moreover, genome wide gene expression profiles of sphere cells relatively to adherent cells revealed an extensive transcriptional reprogramming involving several stemness and cancer-related genes, indicating that transformed cells are highly plastic entities adopting specific gene expression programs depending on different environmental conditions. However, sphere cells were only slightly more tumorigenic *in vivo* than adherent cells suggesting that different subpopulations can support tumorigenicity in transformed cells, highlighting a further level of complexity in tumor heterogeneity.

Biography

Chiara Mondello is Senior Researcher and Group Leader at the Institute of Molecular Genetics of the National Research Council in Pavia (Italy). Her main interests concern the study of genome instability and cellular transformation in mammalian cells. She has published more than 80 papers in peer-reviewed journals and several chapters in books. She has been the Editor of the book "*Multiple Pathways in Cancer Development*" (Transwell Research Network).

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